

CLAIMS:

1. A pharmaceutical preparation, comprising a metal carbonyl compound or pharmaceutically acceptable salt thereof, a guanylate cyclase stimulant or stabilizer and at least one pharmaceutically acceptable carrier.
2. A pharmaceutical preparation according to claim 1, wherein the metal carbonyl makes available CO suitable for physiological effect, for delivery of carbon monoxide to a physiological target.
3. A pharmaceutical preparation according to claim 2, wherein said metal carbonyl compound makes CO available by at least one of the following means:
 - 1) CO derived by dissociation of the metal carbonyl is present in the composition in dissolved form;
 - 2) on contact with a solvent or ligand the metal carbonyl releases CO;
 - 3) on contact with a tissue, organ or cell the metal carbonyl releases CO;
 - 4) on irradiation the metal carbonyl releases CO.
4. A pharmaceutical preparation according to claim 1, 2 or 3, wherein said metal carbonyl compound and said guanylate cyclase stimulant/stabilizer are combined in a single composition.
5. A pharmaceutical preparation according to claim 1, 2 or 3, wherein said metal carbonyl compound and said guanylate cyclase stabilizer/stimulant are in separate compositions for administration simultaneously or sequentially.

6. A pharmaceutical preparation according to any one of the preceding claims wherein the metal carbonyl compound has the formula $M(CO)_x A_y$ where x is at least one, y is at least one, M is a metal, the or each A is an atom or group bonded to M by an ionic, covalent or coordination bond but is not CO , and in the case where $y > 1$ each A may be the same or different, or a pharmaceutically acceptable salt of such a compound.

7. A pharmaceutical preparation according to claim 6, wherein M is a transition metal.

8. A pharmaceutical preparation according to claim 6 or claim 7, wherein A is selected from neutral or anionic ligands, such as halide, or derived from Lewis bases and having N , P , O , S or C as the coordinating atom(s).

9. A pharmaceutical preparation according to any one of claims 1 to 5, wherein the metal carbonyl compound has the formula

$M(CO)_x A_y B_z$ where

M is Fe , Co or Ru ,

x is at least one,

y is at least one,

z is zero or at least one,

each A is a ligand other than CO and is monodentate or polydentate with respect to M and is selected from the amino acids

alanine

arginine

asparagine

aspartic acid

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cysteine
glutamic acid
glutamine
glycine
5 histidine
isoleucine
leucine
lysine
methionine
10 phenylalanine
proline
serine
threonine
tryptophan
15 tyrosine
valine

$[O(CH_2COO)_2]^{2-}$ and
 $[NH(CH_2COO)_2]^{2-}$, and

B is optional and is a ligand other than CO.

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10. A pharmaceutical preparation according to any one of the preceding claims wherein the guanylate cyclase stimulant/stabilizer is YC-1.

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11. A pharmaceutical composition according to any one of the preceding claims adapted for delivery by an oral, intravenous, subcutaneous, nasal, inhalatory, intramuscular, intraperitoneal or suppository route.

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12. A method of introducing a therapeutic agent to a mammal comprising the step of administering a pharmaceutical preparation according to any one of the preceding claims.

13. A method of introducing a therapeutic agent to a mammal comprising:

- a) administering a metal carbonyl; and
- 5 b) administering a guanylate cyclase stimulant or stabiliser.

14. A method according to claim 13, wherein the metal carbonyl makes CO available for physiological effect, for
10 delivery of CO to a physiological target.

15. A method according to claim 14, wherein said metal carbonyl compound makes CO available by at least one of the following means:

- 15 1) CO derived by dissociation of the metal carbonyl is present in the composition in dissolved form;
- 2) on contact with a solvent or ligand the metal carbonyl releases CO;
- 3) on contact with a tissue, organ or cell the
20 metal carbonyl releases CO;
- 4) on irradiation the metal carbonyl releases CO.

16. A method according to any one of claims 13 to 15, wherein the steps of administering the metal carbonyl and
25 guanylate cyclase stimulant/stabilizer are simultaneous.

17. A method according to any one of claims 13 to 15, wherein the steps of administering the metal carbonyl and guanylate cyclase stimulant/stabilizer are sequential.
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18. A method according to any one of claims 13 to 17, wherein the metal carbonyl compound has the formula $M(CO)_x A_y$ where x is at least one, y is at least one, M is

a metal, the or each A is an atom or group bonded to M by an ionic, covalent or coordination bond but is not CO, and in the case where $y > 1$ each A may be the same or different, or a pharmaceutically acceptable salt of such a compound.

19. A method according to claim 18 wherein M is a transition metal.

20. A method according to claim 18 or claim 19, wherein A is selected from neutral or anionic ligands, such as halide, or derived from Lewis bases and having N, P, O, S or C as the coordinating atom(s).

21. A method according to any one of claims 13 to 17 wherein the metal carbonyl compound has the formula

$M(CO)_x A_y B_z$ where

M is Fe, Co or Ru,

x is at least one,

y is at least one,

z is zero or at least one,

each A is a ligand other than CO and is monodentate or polydentate with respect to M and is selected from the amino acids

alanine

arginine

asparagine

aspartic acid

cysteine

glutamic acid

glutamine

glycine

histidine

isoleucine
leucine
lysine
methionine
5 phenylalanine
proline
serine
threonine
tryptophan
10 tyrosine
valine

$[\text{O}(\text{CH}_2\text{COO})_2]^{2-}$ and
 $[\text{NH}(\text{CH}_2\text{COO})_2]^{2-}$, and

B is optional and is a ligand other than CO.

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22. A method according to any one of claims 13 to 21,
wherein the guanylate cyclase stimulant/stabilizer is YC-
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23. A method according to any one of claims 15 to 22,
wherein the metal carbonyl compound and/or the guanylate
cyclase stabilizer/stimulant is administered by an oral,
intravenous, subcutaneous, nasal, inhalatory,
intramuscular, intraperitoneal or suppository route.

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24. A method according to any one of claims 12 to 23,
wherein the metal carbonyl and guanylate cyclase
stimulant/stabilizer are administered to an
extracorporeal body organ.

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25. A method according to any one of claims 12 to 24,
where the administration is for the stimulation of
vasodilation, or for treatment of any of hypertension,

such as acute, pulmonary and chronic hypertension, radiation damage, endotoxic shock, inflammation, inflammatory-related diseases such as asthma and rheumatoid arthritis, hyperoxia-induced injury, apoptosis, cancer, transplant rejection, arteriosclerosis, post-ischemic organ damage, myocardial infarction, angina, haemorrhagic shock, sepsis, penile erectile dysfunction, adult respiratory distress syndrome and inhibition of platelet aggregation.

26. A kit comprising a) a metal carbonyl compound; and b) a guanylate cyclase stimulant/stabilizer.

27. A kit according to claim 26, wherein the metal carbonyl is capable of making available CO suitable for physiological effect.

28. A kit according to claim 27, wherein said metal carbonyl compound makes CO available by at least one of the following means:

1) CO derived by dissociation of the metal carbonyl is present in the composition in dissolved form;

2) on contact with a solvent or ligand the metal carbonyl releases CO;

3) on contact with a tissue, organ or cell the metal carbonyl releases CO;

4) on irradiation the metal carbonyl releases CO.

29. A kit according to claim 26 or claim 27, wherein said metal carbonyl compound and said guanylate cyclase stabilizer/stimulant are in separate compositions for administration simultaneously or sequentially.

30. A kit according to any one of claims 26 to 29,
wherein the metal carbonyl compound has the formula
 $M(CO)_x A_y$ where x is at least one, y is at least one, M is
a metal, the or each A is an atom or group bonded to M by
an ionic, covalent or coordination bond but is not CO ,
and in the case where $y > 1$ each A may be the same or
different, or a pharmaceutically acceptable salt of such
a compound.
31. A kit according to claim 30, wherein M is a
transition metal.
32. A kit according to claim 30 or claim 31, wherein A
is selected from neutral or anionic ligands, such as
halide, or derived from Lewis bases and having N , P , O , S
or C as the coordinating atom(s).
33. A kit according to any one of claims 26 to 29,
wherein the metal carbonyl compound has the formula
 $M(CO)_x A_y B_z$ where
 M is Fe , Co or Ru ,
 x is at least one,
 y is at least one,
 z is zero or at least one,
each A is a ligand other than CO and is monodentate
or polydentate with respect to M and is selected from the
amino acids
- alanine
 - arginine
 - asparagine
 - aspartic acid
 - cysteine
 - glutamic acid

glutamine
glycine
histidine
isoleucine
leucine
lysine
methionine
phenylalanine
proline
serine
threonine
tryptophan
tyrosine
valine

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$[O(CH_2COO)_2]^{2-}$ and
 $[NH(CH_2COO)_2]^{2-}$, and

B is optional and is a ligand other than CO.

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34. A kit according to any one of claims 26 to 33,
wherein the guanylate cyclase stimulant/stabilizer is YC-1.

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35. A kit according to any one of claims 26 to 34,
wherein the metal carbonyl and/or the guanylate cyclase
stabilizer/stimulant is adapted for delivery by an oral,
intravenous, subcutaneous, nasal, inhalatory,
intramuscular, intraperitoneal or suppository route.